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Results of Thyreoid Treatment in Sporadic Cretinism, by Frederick Peterson, M. D., Chief of Clinic, Nervous Department, Vanderbilt Clinic, College of Physicians and Surgeons; formerly Neurologist to the Randall's Island Idiot Asylum, New York; and Pearce Bailey, M. D., Assistant Physician, Nervous Department, Vanderbilt Clinic, College of Physicians and Surgeons; Attending Physician to the Alms House, Work House and Incurable Hospitals, New York.

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Original Articles.

RESULTS OF THYREOID TREATMENT IN SPORADIC CRETINISM.

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CRETINISM or myxœdematous idiocy, since the recognition of its dependence upon non-development of or degenerative changes in the thyreoid gland, has been the subject of considerable experimental treatment with thyreoid preparations by physicians of different countries, chiefly, however, in England and America. We have not been able to find published accounts of the effects of thyreoid treatment in endemic cretinism, and the cases we have collected belong to the class known as sporadic cretinism, of which not a few examples are found in every country. There are rare cases in which the want of development or disease of the thyreoid gland during intra-uterine life is manifested to such an extent that the infants are typically myxœdematous at birth, and are either still-born or survive but a few days. More common are cases in which, while the disorder has its inception previous to birth, the progress is slow, and the child lives for some months or for several years. But the usual history of cases of sporadic cretinism is that of a normal condition for the first few years of life until

about the fourth or fifth year. At this time, in the majority of cases, disease of the thyreoid gland developes and induces either slowly or rapidly, according to the degree of alteration in the gland, the mental and physical changes peculiar to the myxœdema of childhood. These changes differ from those of myxœdema in the adult because of the effects of the disorder upon the organism during its period of development. Common to both phases of myxœdema are the general effects upon nutrition, the general œdema, the thin hair, decaying teeth, anæmia, lowered bodily temperature and intellectual impair-

FIG. 1. Cretin, aged 18 months. Before Treatment.

ment. But in the myxœdema of childhood, the stunting of growth in all directions, bodily and mental, is extraordinarily marked.

A sporadic cretin once seen is ever after easily recognized by the physician. His dwarfish stature, thick limbs, short neck, lordosis, prominent abdomen, flattened and retroussé nose, thick lips, large thick tongue, open mouth, absent or imperfect teeth, face devoid of expression, coarse skin, scanty and generally reddish brown hair, anæmia, supraclavicular swellings, and frequent umbilical hernia, form a picture too distinct to be effaced from the mind. The child

suffers from cold, and the temperature is found to be subnormal. On examination the thyreoid gland may be absent, or may be smaller than normal, or present a goitrous enlargement.

The authors have had seven cases under observation since the thyreoid treatment came into use. Four of these were observed at the Vanderbilt Clinic in the service of Prof. Starr and three at the Randall's Island Hospital for Idiots. The condition is, therefore, somewhat rare. One of the children at the Vanderbilt Clinic was a case of a sporadic cretinism in a negro. Of those studied at

FIG. 2. Six weeks after thyreoid treatment was begun.

the Clinic, two were much improved by treatment, one disappeared from sight before treatment was begun, and one we can report as probably cured. This case we describe in detail as follows :

M. P., male child, aged 18 months, born in the United States of Hungarian Hebrew parents, was brought to the Clinic June 25th, 1895. He was the 5th of five children, the other four being normal in every respect. His hair was reddish brown and thin. He had no teeth. The lips were thick, eyelids and face heavy and puffed. There was slight swelling of the supraclavicular region. The

thyreoid gland was distinguishable, but small and hard. The testicles and scrotum were long. There was umbilical hernia. It was very small for its age. Temperature 97.2° Fahr. at time of examination. Absolutely unable to sit up, stand, walk or turn over. Paid no attention to anything going on about it. Had been taught the words "papa" and "mamma," but had no knowledge of their application That was the extent of his vocabulary. The cretinous

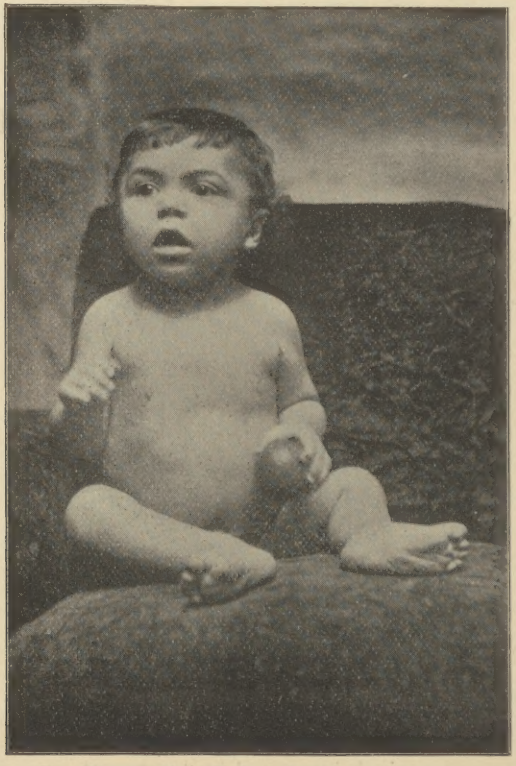

FIG. 3. Seven months after thyreoid treatment was begun.

condition was perfectly distinct, though it had evidently not progressed far. The child had not been treated for its condition. The child was photographed and then put upon one grain of the dried and powdered thyreoid gland of sheep daily, which it has continued to take up to the present time (April, 1896). The second photograph was taken August 14, 1895, about six weeks after beginning

FIG. 4. Cretin, aged 15 years; and normal brother of cretin, aged 4 years. Photograph to illustrate dwarfing of stature in cretinism.

treatment. As is readily seen in the pictures, there was a marked change for the better. The child had become thinner in every respect, had begun to grow; the pendency of the scrotum was less marked; the umbilical hernia had disappeared; the hair had become thicker; two teeth had been cut. The child could sit up on the floor, and had begun to play and laugh with the other children, to understand everything said to it, and to take notice of everything going on about it. Its vocabulary had increased several words. During the past winter the child has had the measles, but has continued its remarkable improvement. The third photograph, taken Jan. 26, 1896, shows a child very intelligent and robust for its age (two years), and in respect to bodily growth, development of teeth and hair, use of language, play, etc., etc., it must now be considered as in every respect a normal child. It is proper to call the case cured, though the thyreoid extract will, no doubt, need to be continued indefinitely.

Our second case observed in the Randall's Island Hospital was a female, aged 15 years, a typical cretin in all respects. The photograph (Fig. 4) shows her dwarfed stature as she stands beside her brother, aged 4 years. Her temperature, taken daily for two weeks previous to treatment, averaged 97° Fahr. She was always cold and kept close to the stove. Her teeth were decayed, her hair thin and red. She paid little attention to her surroundings, and her vocabulary consisted of but two or three words. Treatment was begun with five grains of the dried gland, which proved too much, and it was reduced to one grain daily. Improvement was noticeable in a few days. In the course of three months she grew thinner, gained two inches in height, cut several new teeth, her hair became more abundant, she assumed an intelligent expression, noticed everything about her, played with a doll, and had increased her vocabulary to twenty-seven words. At this time treatment ceased because of changes among internes and attending physicians.

Another cretin in the Idiot Hospital on Randall's Island was so old that he was not treated systematically. The typical cretinous aspect is seen in his photograph (Fig. 5). He is a dwarf, and his age is supposed to be between sixty and eighty somewhere, as he is said to have been a Bowery newsboy forty years ago. He has thin red hair, very few teeth, is now much demented, as he barely responds to his name, and asked his age, says, "nine years." His temperature is subnormal, and he constantly hovers about the stove. Two weeks of thyreoid treatment made no perceptible impression except to improve the temperature and circulation. The age of the

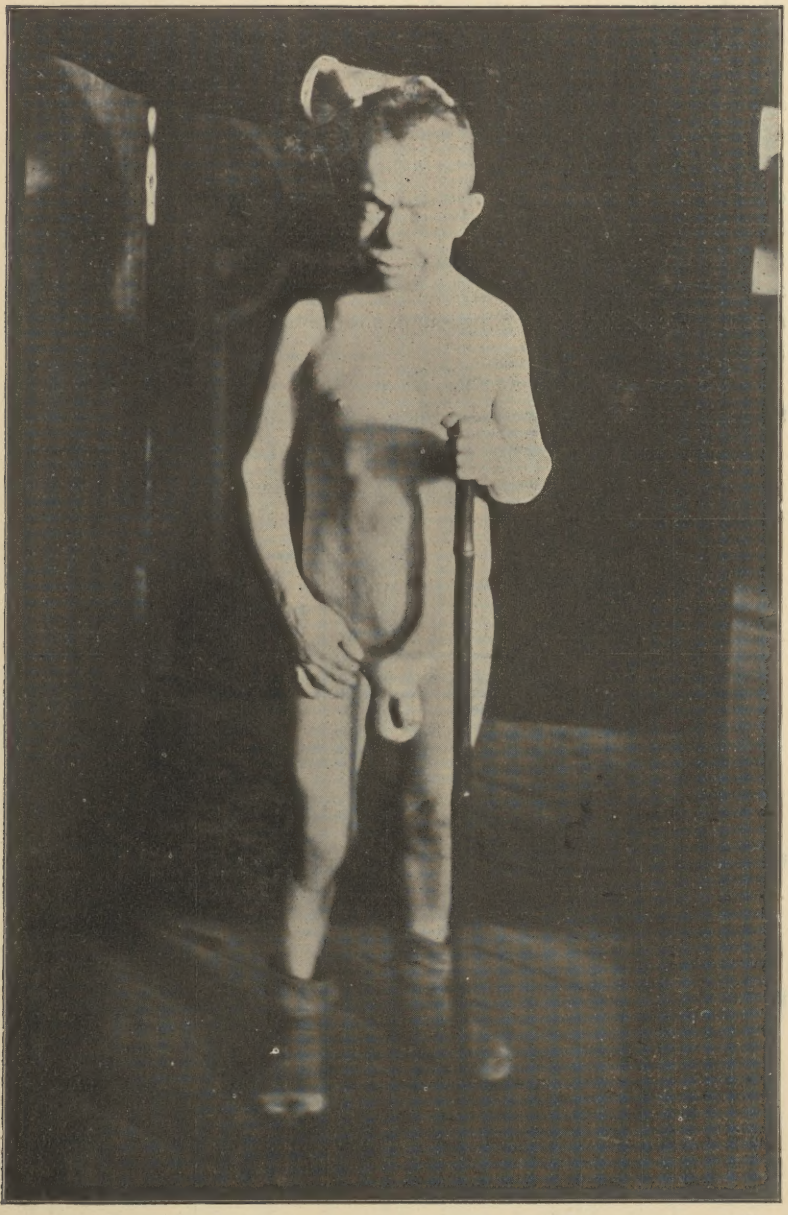

FIG 5. Cretin, aged between 60 and 80 years.

patient would imply a very slow change in the thyreoid gland. The gland is still perceptible though very small.

The cases we have seen illustrate very well the different degrees of cretinism that may be met with. The myxœdematous symptoms, depending as they do directly upon the diminution in the amount of thyreoid secretion, vary from manifestations just perceptible to the experienced eye to symptoms of the most pronounced character. It is no doubt true that there are cases which we may denominate rudimentary cretinism, in which the thyreoid secretion is diminished to so slight a degree that the real condition of some apathetic or feeble-minded and illy nourished child is not recognized. We believe that physicians should be on the lookout for such cases.

We append here a table of all cases of cretinism treated by thyreoid extract that we have been able to find :

TABLE OF PUBLISHED CASES OF CRETINISM TREATED BY THYREOID ADMINISTRATION.

Author and Reference.	Sex.	Age at beginning of Treatment.	Duration of Disease.	Symptoms.	Duration of Treatment.	Character of Treatment.	Results.
Robin. Lyon Med., 1892. LXX., p. 405.	F.	7 yrs.	Congenital	Characteristic. Unable to walk or talk.	Not stated.	Extract, followed by implantation.	Complete change in appearance. Walks.
Carmichael.* Lancet, 1893. I., p. 580.	F.	8½ yrs.	Congenital ?	Characteristic appearance. Intelligence limited. Unable to walk or talk.	9 mos.	Hyp. inject. of extract and feeding of raw gland.	Skin became normal. Learned to walk and run. Intelligence improved.
Evans. Br. Med. Jour. 1893. I., p. 767.	M.	8 yrs.	Not stated.	Not stated.	6 weeks.	One lobe of sheep's thyreoid twice a week.	No improvement.
Hellier.* Lancet, 1893. II., p. 1117.	F.	2½ yrs.	1-2 yrs ?	Characteristic appearance. Unable to walk or talk. Idiotic.	4⅓ mos.	Extract.	Oedematous symptoms gone. More intelligent. Cannot walk or talk.
Lunn. Br. Med. Jour. 1893. p. 1273.	F.	26 yrs.	Not stated.	Idiotic. No other details.	Not stated.	Not stated.	Became relatively intelligent and menstruation was resumed.
Ord.* Lancet, 1893. II., p. 1113.	F.	6½ yrs.	Congenital ?	Characteristic appearance. Could not walk or talk.	8 mos.?	Had been grafted previously with temporary benefit. Raw gland & extract.	Great improvement. Learned to walk in three months. Can talk.
Ibid.*	M.	3 yrs.	Congenital ?	Could not talk. Always dwarfed and bow-legged Skin dry.	8 mos.?	Raw gland, dried gland and extract.	Marked. Learned to talk. Growing rapidly.
Ibid.	M.	9 mos.	Not stated.	Typical.	———	———	Improved rapidly, but died of intercurrent diphtheria.

* Indicates that the original papers are accompanied with photographs.

Author and Reference.	Sex.	Age at beginning of Treatment.	Duration of Disease.	Symptoms.	Duration of Treatment.	Character of Treatment.	Results.
Ibid.*	M.	9⅛ yrs.	In infancy.	Characteristic physically, but intelligent. Height, 34 in. Could walk.	8 mos.?	Compressed extract.	Grew 1⅛ inches in four months. Improvement in other respects not so marked.
Owen. Br. Med. Jour. 1893. p. 1273.	F.	26 yrs.	In infancy	Characteristic. 40¼ inches high.	——	Tabloids.	Improvement.
Patterson. Lancet, 1893. II., p. 1116.	M.	19 mos.	12 mos?	Characteristic.	8 mos.	Extract.	Oedematous symptoms gone. Can stand. Learning to talk. Has sixteen teeth.
Vermehren. Deut. Med. Woch., 1893. p. 256.	F.	29 yrs.	24 yrs.	Characteristic.	3 weeks.	Thyreodin.	Marked improvement.
Wood. Aust. Med. J., 1893. p. 166.	F.	1 yr. 11 mos.	——	——	1 mo.	Had been grafted. Raw gland.	One month's feeding without benefit.
Rehn. Ver der XII. Cong., 1893. p. 224.	F.	4⅛ yrs.	Not stated.	Characteristic.	2 mos.	Extract.	Marked improvement.
Ibid.	F.	6⅛ yrs.	Not stated.	Characteristic.	2 mos.	Extract.	Marked improvement.
Anson. Lancet, 1894. I., p. 1063.	F.	10 yrs.	Congenital	Characteristic appearance. Could walk clumsily. Mental process slow	1 yr.	Raw gland and glycerine extract.	Oedematous symptoms gone. Intelligence improved. Grew 4 in. (For 3 yrs. previously had grown only 2 inches.)
Bramwell.* Br. Med. Jour. 1894. I., p. 6.	F.	16½ yrs.	Not stated.	Typical. Idiotic. 29⅛ inches high	6 mos.	Extract and tabloids.	Oedematous symptoms disappeared More intelligent Grew 6½ inches.
Comby. Med. Infant., 1894. I., p. 578.	F.	2 yrs.	6 mos.	Characteristic appearance. Cannot walk or talk.	15 days	Raw gland.	Improvement.
Crary.* Am. Journal Med. Science, 1894. p. 529.	F.	5 yrs.	3 mos.	Characteristic appearance. Dwarfed, lordosis, impaired intelligence.	2½ mos.	Extract.	Great improvement mentally and physically.
Garrod.† Br. Med. Jour. 1894. II., p. 1112.	F.	8½ yrs.	Not stated.	Characteristic.	1½ yrs.	Not stated.	Lost cretinoid appearance. Grew 5 inches.
Lendon. Aust. M. Gaz., 1894. p. 134.	F.	12 yrs.	Not stated.	32 in. in height. 25 lbs. in weight. Loss of sphincter control.	17 days	Hypoder. inject. of extract.	Improvement—then fever, bronchitis death.
Ibid.	F.	18 yrs.	Not stated.	Height, 3 ft. 3¾ in. 2¾ in. only growth in 6 yrs.	9 mos.	Not stated.	Grew 4⅜ inches.
Northrup. N. Y. Med. J., 1894. 60, p. 505.	F.	9 yrs.	8 yrs.	Characteristic. Idiotic.	80 days	Extract.	Much improved.
Ibid.	Not stated.	12 yrs.	Not stated.	Characteristic.	Not stated.	Not stated.	Results not marked.

* Indicates that the original papers are accompanied with photographs.

Author and Reference.	Sex.	Age at beginning of Treatment.	Duration of Disease.	Symptoms.	Duration of Treatment.	Character of Treatment.	Results.
Osler. N. Y. Med. J., 1894. 60, p. 505.	M.	3 yrs.	Not stated.	Characteristic. Could not walk or talk.	14 mos.	———	Oedematous symptoms all disappeared. Walks and talks. Grew 4 inches.
Ibid.	M.	19 yrs.	Not stated.	Not stated.	———	Treatment not systematically carried out.	No material gain.
Railton.* Br. Med. Jour. 1894. I., p. 1180.	M.	14 yrs.	Not stated.	Characteristic. Idiotic. 33 inches high.	11 mos.	Raw gland and tabloids.	Oedematous symptoms disappeared. Cannot talk well. Grew 3 inches.
Smith.* Br. Med. Jour. 1894. I., p. 1178.	M.	9 yrs.	7 yrs.	Not a severe case.	9 mos.	Raw gland and tabloids.	Improvement.
Thomson.* Edin. Med. J., 1894. Feb'y, p. 720.	M.	18 yrs.	16 yrs.	Characteristic. Mind that of a child of 3 years. 33½ inches high. Waddling gait.	12 mos.	Raw gland.	Some toxic symptoms. Skin grew softer and mind became brighter. Grew 4¾ in. Most improvement at first.
Escherich. Wien. Med. Woch., 1895. p. 350.	F.	6½ yrs.	4½ yrs?	Myxoedematous symptoms not marked. "A backward child."	6 mos.	Raw gland of calf.	Grew 13 centimeters.
Lebreton. Gaz. Med. de Paris, 1895. No. 1, p. 8.	M.	13 yrs.	12 yrs.	Characteristic. Idiotic.	Not stated.	Raw gland, slightly browned.	Dentition appeared. Growth resumed. Nothing said of intelligence.
No. 3, p. 31.	M.	3 yrs.	1 yr.	Characteristic.	1 yr.	Dried gland.	Improved.
Sinkler.* Int. Med. Mag. 1894-5. III., p. 785.	F.	4 yrs.	3½ yrs.	Characteristic. Unable to walk, talk or understand. 30 2-8 in. high.	3 mos.	Extract.	Oedematous symptoms mostly disappeared. Became more intelligent and began to talk. Grew 2¼ in.
West.* Arch. of Paed. 1895. p. 348.	F.	17 mos.	Congenital	Stupid. 23¼ in. high. Weight, 14½ lbs. No teeth.	6 mos.	Dessicated extract. Glycerine extract.	Oedematous symptoms disappeared. Intelligent. Eight teeth. Grew 4 inches.
Fruitnight. Arch. of Paed. 1896. p. 143.	M.	4 yrs.	3 yrs.	Cannot walk or talk. Weight, 16½ lbs. Height, 25 in.	1 mo.	Dried gland.	Grew thinner and more intelligent.
Noyes.* N. Y. Med. J., 1896. 68, p. 334.	F.	2 yrs.	1 5-6 yrs.	Characteristic. Length, 24 in.	4½ mos.	Tablets.	Oedematous symptoms gone. Intelligence improves. Begun to creep. Grew 8 inches.
Parker.* Br. Med. Jour. 1896. I., p. 333.	F.	6½ yrs.	Congenital ?	Typical.	12 mos.	Tabloids.	Oedematous symptoms disappeared. Learned to walk. Did not learn to talk.
Peterson.* (Present article.)	M.	18 mos.	?	See this article.	Now 10 mos.	One grain extract daily.	Probably cured. (See report in this article.)
Peterson.* (Present article.)	F.	15 yrs.	?	See this article.	3 mos.	One grain extract daily.	Great improvement. (See report in this article.)
Vinke.* Med. News, 1896. 68, p. 309.	M.	6 yrs.	Congenital	Characteristic appearance. Can walk and talk a little.	5 mos.	Tablets.	Marked improvement in all symptoms.

* Indicates that the original papers are accompanied with photographs.

† Same author reports two other cases not so much improved.

The above table contains most, if not all, of the cases of sporadic cretinism, treated with thyreoid, which have been reported with sufficient detail to render them valuable for statistical purposes. From this summary it appears that under thyreoid treatment the symptoms of myxœdema disappear from the child quite as readily as from the adult. In none of the cases quoted did the general œdematous symptoms fail to yield to the remedy, when it was properly and sufficiently applied. The skin became soft, the swellings disappeared and the whole appearance of the patient was completely changed.

The carrying out of the treatment of myxœdema is attended with fewer difficulties and dangers in children than in adults. Toxic symptoms have been observed in a few cases only, and but two have died under treatment. Of these one died of intercurrent diphtheria and one of bronchitis; in neither of these two cases was the treatment regarded as a causative factor of the fatal symptoms.

In addition to the disappearance of the symptoms from the skin and subcutaneous tissues the treatment of sporadic cretinism has in some cases met with brilliant results by permitting a return of development and growth to children in whom these functions had been limited or arrested by the disease. But although marked changes in the mental and physical condition of cretins have occurred, it yet remains to be reported that these cases become the physical and intellectual equals of children who have never had myxœdema.

Improvement consequent upon a return of development has been more constant in the body than in the brain. A large number of the reported cases have grown considerably taller and have acquired sufficient power and control of the limbs to enable them to walk, which had previously been impossible. The teeth, which have been absent or defective, begin to appear normally.

Intellectual progress has been neither so constant nor so rapid. In nearly all the cases there has been noted some mental improvement, but in only a few has the power of speech been acquired when it previously had been absent.

The occurrence, in the formative period of infancy and childhood, of a disease which attacks fundamentally nutrition, development and growth, has much more disastrous effects than when its appearance is delayed until the organism has reached maturity.

And while it is possible that the removal of causes inhibitory to growth may result in a gradual return of developmental processes, the thyreoid treatment of infantile myxœdema has in no case been

carried out for a sufficient length of time to permit the assertion that such will be the case. We have been able to find no case in which treatment is reported to have lasted more than a year and one-half, and of no case is it said that the patient was, in all respects, cured. But from the fact that in nearly all of the cases treatment was not instituted until the child was several years of age and had developed but little or not at all for a considerable length of time, several years would be necessary, by the natural processes of development, for the complete re-establishment of normal growth.

Although data sufficient to justify positive assertions are lacking it seems entirely in the range of possibility that if the treatment of sporadic cretinism were begun at the outset of the disease, before growth was seriously interfered with, it would permit the proper development of the child, without myxœdematous symptoms, as long as the thyreoid was administered.

These questions must find their solution in the future when the thyreoid treatment will have been used for a time sufficiently long to justify conclusions as to the extent and permanency of its value.

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